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From: **Zeba Ali** Date January 28, 2008

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Client/Matter: U.S. Patent Application Serial No. 10/650,211
Our Ref.: 2839/46001

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Examiner Soroush	**US Patent and Trademark Office**	**571 271 5008**	

This declaration is a draft and for discussion purposes only. The people going on the interview will be

Dr. Nicholas Franks (co-inventor)

Zeba Ali (attorney representing Applicant) and

William Jones (in-house counsel for Applicant).

Zeba Ali

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PAGE 1/5 * RCVD AT 1/28/2008 4:23:50 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-5/8 * DNIS:2738300 * CSID:2022204201 * DURATION (mm-ss):01-32

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT	:	Petzelt *et al.*
SERIAL NO.	:	11/650,211
FILED	:	January 04, 2007
FOR	:	USE OF XENON FOR TREATING NEUROINTOXICATIONS
EXAMINER	:	Soroush, Layla
Docket No.	:	AGALIN 3.3-002 DIV CON
GROUP ART UNIT	:	1617

COMMISSIONER FOR PATENTS
P.O. BOX 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. 1.132

SIR:

I, Dr. _____, declare as follows:

1. I am _____, a position I have held since _____. Prior to that I _____

2. I received a _____degree from _____in December 1970.

3. I have authored several journal articles involving the study of xenon in mammalian subjects at various stages of development. A full list of my publications is set forth in my *curriculum vitae*, attached as Exhibit A.

PAGE 2/5 * RCVD AT 1/28/2008 4:23:50 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-6/8 * DNIS:2738300 * CSID:2022204201 * DURATION (mm-ss):01-32

4. I have reviewed the above-identified application, which is directed to methods of treating ischemia in a mammal comprising administering to a mammal suffering from ischemia a therapeutically effective amount of xenon to treat the ischemia.

5. I am familiar with the Office Actions dated June 26, 2007 and November 26, 2007, as well as the references cited therein: Radue & Kendall, Neuroradiology, Vol. 16, pp 224-227 (1978) (hereinafter "Radue"); and U.S. Patent No. 5,357,959 to Fishman (hereinafter "Fishman").

6. It is my opinion that Radue describes the use of xenon as a contrast agent for the computer tomographic imaging of tumors and ischaemic lesions. (*See* page 242, column 1). Further, it is my opinion that Fishman describes the use of xenon as a contrast agent in diagnostic medical magnetic resonance imaging. (*See* Abstract). Neither of these two references, alone or in combination, discloses or suggests the therapeutic treatment of patients suffering from ischemia by administering xenon as recited by the claims of the present application.

7. In accordance with my own understanding of Radue, the Examiner acknowledges that "Radue teaches xenon as a contrast agent in computer tomography for diagnostic purposes in patients." (*See* November 26, 2007 Office Action, page 5, paragraph 3). However, the Examiner further states that Radue also stands for the proposition that xenon can be used to treat ischemias therapeutically. (*See* November 26, 2007 Office Action, page 5, paragraph 3). The Examiner's notion seems to be based on Radue's description of a single patient (out of seven analyzed) whose ischaemic lesions take up xenon in a normal manner and who recovers clinically some time after xenon has been administered to better detect these lesions.

8. It is my opinion that Radue cannot reasonably be read in this way. For example,, Radue itself contains no explicit statement that there is a causal relationship between the administration of xenon and the clinical recovery of one patient. Moreover, the overall

PAGE 3/5 * RCVD AT 1/28/2008 4:23:50 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-5/8 * DNIS:2738300 * CSID:2022204201 * DURATION (mm-ss):01-32

focus of this reference is the diagnostic use of xenon. This reference does not concern itself at all with the therapeutic use of xenon or even therapeutic issues in general. Further, Radue, in addition to what I have outlined above, discloses that penetration of xenon into tissue is reduced by a reduced blood flow into that tissue or by tissue abnormalities arising from an ischaemic event. (*See* page 227, column 1, paragraph 4 *et seq.*) Thus, there is an inverse relationship between the severity of the consequences of an ischaemic event and the extent as to which xenon penetrates the affected tissue.

9. The Examiner relies on a single patient (Case 7 in Table 1) with an ischaemic partial lesion, who was reported to have made a complete clinical recovery. (*See* Radue at abstract and pages 224). However, Radue makes clear that while plain CT showed a low attentuation lesion, "xenon uptake was normal" for the patient throughout. (*See* Radue at pages 224 and 227). Further, Table 1 indicates that the xenon uptake in the infarct region of that patient was not statistically different than the normal side of the brain. In contrast, the xenon uptakes for the other patients, none of which were reported to make such a reovery, were significantly lower.

10. Based on all the foregoing, the most reasonable conclusion, and the most scientifically sound one, would be that the sole patient who recovered suffered from ischaemic lesions that were less severe than the lesions found in the other six patients which were also examined. This, in turn, would lead one to conclude that the patient recovered because his ischaemic lesions were relatively minor, and not because xenon had a therapeutic effect.

11. Furthermore, consideration must be given to the small size of the patient group analyzed and its heterogeneous nature. A group of seven patients that have ischaemic lesions of dramatically different age and size does simply not allow a reasonable conclusion to be drawn as to the relationship between a patient's treatment with xenon and the likelihood of his recovery from an ischemic event. The data provided in Radue give absolutely no assurance that a similar result, i.e., clinical recovery of a patient having ischaemic lesions,

PAGE 4/5 * RCVD AT 1/28/2008 4:23:50 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-5/8 * DNIS:2738300 * CSID:2022204201 * DURATION (mm-ss):01-32

can be reached by others at a later time. Finally, based only on Radue, one would not reasonably think that clinical recovery is a necessary, invariable occurrence once xenon has been administered to a patient suffering from ischaemic lesions, particularly since Radue focuses only on the use of xenon as a diagnostic. If anything, the data in Radue teach away from the therapeutic use of xenon because there is no indication that any of the other patients in the limited study recovered.

12. For at least these reasons, it is my opinion that Radue does not disclose or suggest the therapeutic use of xenon to treat patients suffering from ischemia. It is also my opinion that Fishman does not disclose or suggest the therapeutic use of xenon either as Fishman is directed to the use of xenon as a contrast agent in diagnostic procedures.

13. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the patent or any reexamination certificate issued therefor.

Dated: _____ _____

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PAGE 5/5 * RCVD AT 1/28/2008 4:23:50 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-5/8 * DNIS:2738300 * CSID:2022204201 * DURATION (mm-ss):01-32